

REMARKS

The Official Action dated April 4, 2005 has been carefully reviewed. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At page 2 of the Official Action, the Examiner has objected to the specification for containing minor informalities. Applicants have amended the specification to recite the correct priority claim and have inserted sequence identifiers where appropriate into the specification, thereby rendering these objections moot.

Claims 1-22 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Claims 1-22 have also been rejected under 35 U.S.C. §112, first paragraph. It is the Examiner's position that undue experimentation would be required to practice the invention as claimed.

The foregoing constitutes the entirety of the objections and rejections raised in the April 4, 2005 Official Action. In light of the amendments to the claims and the following remarks, each of the above-noted rejections under 35 U.S.C. § 112, first and second paragraphs, is respectfully traversed. Applicants submit that the claims as presently amended are in condition for allowance.

**THE METES AND BOUNDS OF CLAIMS 1-22 AS AMENDED ARE CLEAR TO
ONE OF ORDINARY SKILL IN THE ART**

The Examiner has rejected claims 1-22 as allegedly indefinite. The relevant inquiry in determining whether a given claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is whether the claim sets out and circumscribes a particular area with a reasonable degree of

precision and particularity such that the metes and bounds of the claimed invention are reasonably clear. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971). Applicants respectfully submit that with respect to claims 1-22 of the present application, such inquiry must be answered in the affirmative. However, in order expedite issuance of the present application, the claims have been amended as set forth below.

The Examiner contends that the phrase "protein having excision activity" in claims 1 and 13 renders the metes and bounds of the claims unclear. Applicants have employed the Examiner's helpful suggestion and replaced the phrase with the "site-specific recombinase having excision activity".

The phrase "thereby excising said predetermined sequence" is also found objectionable by the Examiner. Specifically, the Examiner asserts that the claims do not clearly indicate what the predetermined target sequence is. Applicants respectfully disagree. The skilled person in this art area appreciates that the predetermined sequence to be removed is any sequence which is flanked by the excision sites acted on by the recombinase of step a) and exemplified by the CRE-LOX containing constructs described in the present application. It is respectfully submitted that the amendment to steps b) and e) of claim 1 requiring the sequence for removal to be flanked by excision sites removes any perceived ambiguity from the claims. The Examiner also suggests that Applicants remove the recitation of "at a predetermined target sequence such that excision sites flank said predetermined target sequence following homologous recombination" in claim 13. Applicants submit this aspect of the method of the invention is described in Example 4. Plastid transformation as described herein is mediated by homologous recombination. The sequence of the plastid genome is known for most, if not all plants. The construct in step b) of claim 13 can be designed to contain the plastid gene targeted for deletion as the optional gene of interest and a selectable marker gene which are each flanked

by excision sites which are in turn flanked by plastid targeting nucleic acid sequences which facilitate homologous recombination into the plastid genome targeted for transformation. Upon transformation, such a construct would replace the native sequence of the gene to be deleted with the modified sequence and would also include the selectable marker gene, both of these being flanked by excision sites.

Following introduction of the construct of step a) into such plant cells, both the selectable marker gene and the plastid gene targeted for deletion would be excised.

Regarding the Examiner's assertion that it is unclear if the excision sites of line 7 of step b) are the same as those recited in line 3, it is respectfully submitted that the claim as drafted is clear. However, the claim has been amended to recite "said excision sites" thereby clarifying the meaning of the claim.

Claim 13 has been amended to include the "phrase "the plant of" as suggested by the Examiner. Claims 11 and 19 have also been amended to insert the phrase "of the plant of" as suggested by the Examiner.

The Examiner has objected to claim 15 for reciting the term "associated". The claim has been amended to delete this term thereby rendering this rejection moot.

Claim 20 has been amended to recite "the constructs" thereby clarifying the meaning of the claim.

The Examiner contends that it is unclear whether the plants of claims 21 and 22 comprise the first and second DNA constructs minus the predetermined target sequence.

Applicants submit that it is clear that the present claims clearly recite that the resulting plants lack the either the selectable marker gene and/or the plastid sequence targeted for deletion. The plants may or may not contain the first construct depending on the type of nuclear plant transformation method employed. As set forth at page 35, lines 20 to 25, the recombinase may be stably integrated into

the nuclear genome, expressed transiently or under the control of an inducible promoter.

In light of the foregoing amendments and remarks, it is respectfully submitted that the metes and bounds of the claims are clear to those of skill in the art of the creation of transplastomic plants. Accordingly, it is respectfully requested that the rejection of claims 1-22 under 35 U.S.C. §112, second paragraph be withdrawn.

**CLAIMS 1-22 AS AMENDED ARE FULLY ENABLED BY THE
DISCLOSURE IN THE SPECIFICATION**

The Examiner has rejected claims 1-22 asserting that the specification fails to enable methods where the first construct lacks a plastid targeting sequence and the nucleic acid contained therein is not encoding a site specific recombinase. The claims have been amended to replace the phrase "protein having excision activity" with "site specific recombinase". Additionally, claims 1 and 13 have been amended to remove the term "optional". It is respectfully submitted that the skilled person could readily practice the instantly claimed methods without resorting to undue experimentation.

The Examiner asserts that claim 13 as written is not enabled by the specification. Specifically, the Examiner asserts that "no scenario is taught in the specification in which lox sites flank a predetermined target sequence present in the plastid genome itself following integration into the genome". Thus the Examiner contends that it is unclear how the lox sites could then flank the predetermined sequence following integration.

A rejection under 35 U.S.C. §112, first paragraph, based on inadequate enablement is proper only when the rejected claim(s) is (are) of such breadth as to read on subject matter to which the specification is not enabling. In re Borkowski, 164 U.S.P.Q. 642 (CCPA 1970). Moreover, it is settled law that whenever the adequacy of enablement provided by an applicant's specification is challenged, the PTO has the

initial burden of giving reasons, supported by the record as a whole, why the specification is not enabling. In re Armbruster, 185 U.S.P.Q. 152 (CCPA 1975). Indeed, a properly supported showing that the disclosure entails undue experimentation is part of the PTO's initial burden under §112, first paragraph. In re Angstadt, 190 U.S.P.Q. 214 (CCPA 1976).

As discussed above in connection with the rejection of claim 13 for alleged indefiniteness, the methods of the invention clearly enable the skilled artisan to delete a preselected target sequence from the plastid genome. Because the plastid genome sequence is known and homologous recombination in the plastid genome occurs readily, such a method could be readily performed as discussed above. Example 4 describes such a method and Figure 20 provides a construct for targeted deletion of the clp gene for example. Applicants submit that this aspect of the methods of the invention is fully disclosed and enabled by the specification.

The Examiner also asserts that claims 6 and 7 read on excision sites recognized by two different recombinases and therefore cannot be implemented without undue experimentation. The claims have been amended to include reference to the recombinase employed thereby fully enabling the claimed subject matter.

In light of all the remarks and foregoing claim amendments, it is respectfully requested that the rejection of claims 1-22 for inadequate enablement be withdrawn.

In view of the amendments presented herein and the foregoing remarks, it is respectfully urged that all of the rejections set forth in the April 4, 2005 Official Action be withdrawn and that this application be passed to issue. In the event that the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issue may be resolved through a telephone interview, the Examiner is requested to contact the undersigned attorney at

the phone number given below.

Respectfully submitted,
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